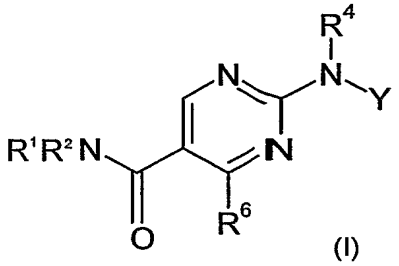
Claims

1. A method of treating a human or animal subject suffering from a condition which is mediated by the activity of CB2 receptors or a condition which is mediated by PDE4 which comprises administering to said subject a therapeutically effective combination of one or more CB2 modulators and one or more PDE4 inhibitors.

2. The use of a combination of one or more CB2 modulators and one or more PDE4 inhibitors in the treatment of a disease mediated by CB2 receptors or PDE4.

3. The use of a combination of one or more CB2 modulators and one or more PDE4 inhibitors in the manufacture of a medicament for treating a disease mediated by CB2 receptors or PDE4

4. The method according to claim 1 or the use according to claim 2 or claim 3, in which the CB2 modulator is selected from a compound of formula (I):



(I)

wherein

Y is phenyl, optionally substituted with one, two or three substituents;

R^1 is selected from hydrogen, C_{1-6} alkyl, C_{3-6} cycloalkyl and halosubstitutedC_{1-6} alkyl;

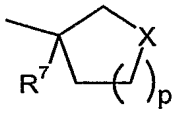
R^2 is $(CH_2)_mR^3$ where m is 0 or 1;

or R^1 and R^2 together with N to which they are attached form an optionally substituted 4- to 8- membered non-aromatic heterocyclyl ring;

R^3 is an optionally substituted 4- to 8- membered non-aromatic heterocyclyl group, an optionally substituted C_{3-8} cycloalkyl group, an optionally substituted straight or branched C_{1-10} alkyl, a C_{5-7} cycloalkenyl or R^5;

R^4 is selected from hydrogen, C_{1-6} alkyl, C_{3-6} cycloalkyl, or halosubstitutedC_{1-6} alkyl, $COCH_3$, and SO_2Me;

R^5 is



wherein p is 0, 1 or 2 and X is CH_2, O, S, SO or SO_2;

R^6 is methyl, chloro or CHxFn wherein n is 1, 2, or 3, x is 0, 1 or 2 and n and x add up to 3;

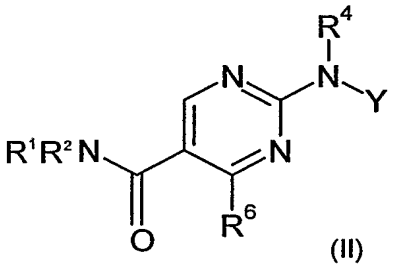
R^7 is OH, C_{1-6}alkoxy, $NR^{8a}R^{8b}$, $NHCOR^9$, $NHSO_2R^9$, $SOqR^9$;

R^{8a} is H or C_{1-6}alkyl;

R^{8b} is H or C_{1-6}alkyl;

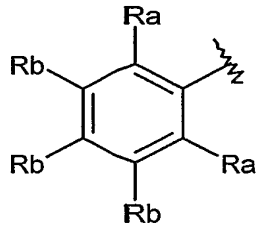
R^9 is C_{1-6}alkyl; and
q is 0, 1 or 2;

or a compound of formula (II):



(II)

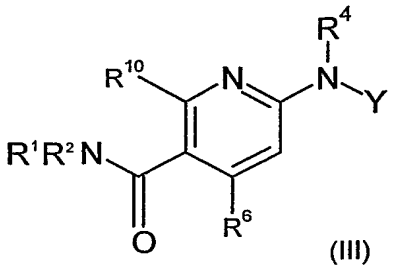
wherein
Y is phenyl, substituted with one, two or three substituents;
R^1 is selected from hydrogen, C_{1-6} alkyl, C_{3-8} cycloalkyl, and halosubstitutedC_{1-6} alkyl;
R^2 is $C(R^7)_2R^3$;
R^3 is an optionally substituted 5- to 6- membered aromatic heterocyclyl group, or group A:



(A)

R^4 is selected from hydrogen, C_{1-6} alkyl, C_{3-7} cycloalkyl, and halosubstitutedC_{1-6} alkyl, $COCH_3$, or SO_2Me;
R^6 is methyl, chloro or CHxFn wherein n is 1, 2, or 3, x is 0, 1 or 2 and n and x add up to 3;
Ra can be independently selected from hydrogen, fluoro, chloro or trifluoromethyl;
Rb can be independently be selected from hydrogen, C_{1-6} alkyl, C_{1-6} alkoxy, haloC_{1-6} alkoxy, hydroxy, cyano, halo, sulfonyl, $CONH_2$, COOH or $NHCOOC_{1-6}$alkyl; and
R^7 can be independently hydrogen or C_{1-6} alkyl,
with the proviso that the compound is not
2-(4-*tert*-butyl-phenylamino)-4-trifluoromethyl-pyrimidine-5-carboxylic acid benzylamide;
2-(4-*tert*-butyl-phenylamino)-4-trifluoromethyl-pyrimidine-5-carboxylic acid benzyl-methyl-amide;
2-(3-Chloro-phenylamino)-4-trifluoromethyl-pyrimidine-5-carboxylic acid 2-methoxy-benzylamide; or
2-(3-Chloro-phenylamino)-4-trifluoromethyl-pyrimidine-5-carboxylic acid 2-bromo-benzylamide;

or a compound of formula (III):



(III)

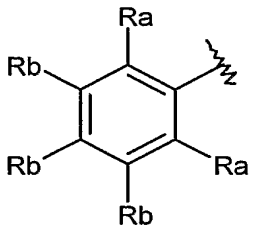
wherein

Y is phenyl, substituted with one, two or three substituents;

R^1 is selected from hydrogen, C_{1-6} alkyl, C_{3-7} cycloalkyl, or halosubstitutedC_{1-6} alkyl;

R^2 is $(CH_2)mR^3$;

R^3 is an unsubstituted or substituted 5- to 6- membered aromatic heterocyclyl group, or group A:



(A)

R^4 is selected from hydrogen, C_{1-6} alkyl, C_{3-7} cycloalkyl, or halosubstitutedC_{1-6} alkyl, $COCH_3$, and SO_2Me;

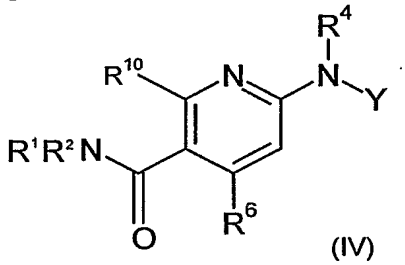
R^6 is unsubstituted or substituted (C_{1-6})alkyl or chloro and R^{10} is hydrogen or R^{10} is unsubstituted or substituted (C_{1-6})alkyl or chloro and R^6 is hydrogen;

Ra can be independently selected from hydrogen, fluoro, chloro or trifluoromethyl;

Rb can independently be selected from hydrogen, C_{1-6} alkyl, C_{1-6} alkoxy, halo substituted C_{1-6} alkoxy, hydroxy, cyano, halo, sulfonyl, $CONH_2$, COOH, SO_2CH_3, $NHCOCH_3$, $NHSO_2CH_3$ and $CONHCH_3$; and

m is 1 or 2;

or a compound of formula (IV):



(IV)

wherein

Y is phenyl, unsubstituted or substituted with one, two or three substituents;

R^1 is selected from hydrogen, C_{1-6} alkyl, C_{3-6} cycloalkyl, or halosubstitutedC_{1-6} alkyl;

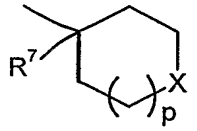
R^2 is $(CH_2)_mR^3$ where m is 0 or 1;

or R^1 and R^2 together with N to which they are attached form an optionally substituted 4- to 8- membered non-aromatic heterocyclyl ring;

R^3 is a 4- to 8- membered non-aromatic heterocyclyl group, a C_{3-8} cycloalkyl group, a straight or branched C_{1-10} alkyl, a C_{2-10}alkenyl, a C_{3-8}cycloalkenyl, a C_{2-10}alkynyl, or a C_{3-8}cycloalkynyl any of which can be unsubtituted or substituted or R^5;

R^4 is selected from hydrogen, C_{1-6} alkyl, C_{3-6} cycloalkyl, or halosubstitutedC_{1-6} alkyl, $COCH_3$, or SO_2Me;

R^5 is



wherein p is 0, 1 or 2, and X is CH_2, O, or S;

R^6 is a substituted or unsubstituted (C_{1-6})alkyl or chloro and R^{10} is hydrogen or R^{10} is a substituted or unsubstituted (C_{1-6})alkyl or chloro and R^6 is hydrogen;

R^7 is OH, C_{1-6}alkoxy, $NR^{8a}R^{8b}$, $NHCOR^9$, $NHSO_2R^9$ or $SOqR^9$;

R^{8a} is H or C_{1-6}alkyl;

R^{8b} is H or C_{1-6}alkyl;

R^9 is C_{1-6}alkyl; and

q is 0, 1 or 2;

or a pharmaceutically acceptable derivative thereof.

5. A method according to claim 1 or the use according to claim 2 or claim 3 in which the PDE4 inhibitor is selected from cilomilast, AWD-12-281, NCS-613, D-4418, CI-1018, V-11294A, roflumilast or T-4401, and pharmaceutically acceptable derivatives thereof.

6. The method of claim 1 or the use of claim 2 or claim 3 wherein the condition is an immune disorder, an inflammatory disorder, pain, rheumatoid arthritis, multiple sclerosis, osteoarthritis, osteoporosis, lung disorders, for example asthma, bronchitis, emphysema, allergic rhinitis, respiratory distress syndrome, pigeon fancier's disease, farmer's lung, chronic obstructive pulmonary disease, (COPD) and cough, or a disorder which can be treated with a bronchodilator.

7. A pharmaceutical composition comprising one or more CB2 modulators and one or more PDE4 inhibitors adapted for use in human or veterinary medicine.